bring the specification into compliance in accordance with Item 4 of the Detailed Action.

With respect to the claims, claims 3, 8, 10, 12, 14-15 and 20 have been canceled and claims 1-2, 9, 21 and 23 have been amended. Claims 1-2, 5-7, 9, 11, 16-19 and 21-23 remain under consideration in this application, claims 4 and 13 having previously been canceled and claim 24 having been deemed withdrawn from consideration as being directed to a non-elected species.

With regard to Items 6-8 in the Detailed Action, claim 20 has been deleted and, in 21, the term "modulating the immune response" in line 1, has been replaced by the term "stimulating cell lysis". In claim 23, line 3, "subject" has been replaced by -- target cell --. This is further believed to overcome a second rejection of the claim under 35 USC § 112 in Item 15B. The amendments to claim 21 from which claims 22 and 23 depend is clearly supported in the specification. See, for example, Example 1 in the specification and particularly at page 12, paragraph 3 and in Example 2 at page 13, paragraph 4. It is believed now that these claims are adequately supported in the specification and that no new matter has been added.

The amendments to claims 1 and 2 are also believed well supported by Examples 1 and 2 and introduce no new matter. The amended claims are now directed only to chimaeric polypeptides and methods for cell lysis as fully described and supported by

Examples 1 and 2 of the present invention so that it is believed that the new matter rejection of Item 13 should be withdrawn. In this regard, it is believed that the experimental result shown on page 12, paragraph 2, and page 13, paragraph 3, really indicate that the inventors had possession of the claimed invention at the time the application was filed.

Other conforming amendments to claim 1 have believed to overcome the remaining rejections based on 35 USC § 112 enumerated in Item 13.

With respect to the rejection on the merits, the amended claims are believed novel because none of the cited documents disclose a molecule as claimed in claim 1 including the required sequence. It is further believed that the rejection based on 35 USC § 103(a) based on Casten et al, in view of Fawell et al and Noguchi et al has also been overcome. A careful review of these references reveals no indication in the cited documents, taken either singularly or in combination, that the Shimaeric polypeptide would be processed by the cells in a way such that at least one of the resulting fragments is recognizable by CTLs.

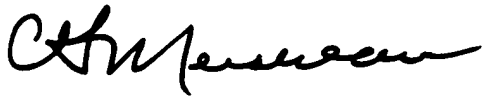
Given the above amendments, taken together with the explanatory remarks contained herein, applicants believe that the requirements and rejections with respect to the present application have been fully met and reconsideration and allowance of the present claims is respectfully requested.

application have been fully met and reconsideration and allowance of the present claims is respectfully requested.

Should issues remain which in the opinion of the Examiner can be resolved by telephone interview, the Examiner cordially requested to contact the undersigned attorney in order to resolve same and expedite prosecution of this application.

Respectfully submitted,

NIKOLAI & MERSEREAU, P.A.



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CERTIFICATE OF MAILING

I hereby certify that the foregoing Amendment in response to the Office Action of October 31, 2001, a Petition for a three-month Extension of Time in application Serial No. 08/737,457, filed on March 12, 1997 of Donald L.N. Cardy et al., entitled "IMPROVEMENTS IN OR RELATING TO PEPTIDE DELIVERY", and a transmittal letter are being deposited with the U.S. Postal Service as First Class mail in an envelope addressed to The Commissioner of Patents and Trademarks, Washington, D.C. 20231, on April 15, 2002.

Barbara L. Davis
Secretary to C. G. Mersereau

Date of Signature: April 15, 2002

Marked-up Version of the Specification Being Amended

On page 11, please replace the first paragraph with the following paragraph:

The oligonucleotides P53-U and -L (encoding the p53 CTL reactive peptide KYICNSSCM SEQ ID NO. 7 (Noguchi et al., 1994 Proc. Natl. Sci. USA 91, 3171-3175) and FLU-U and -L (encoding the influenza A matrix protein peptide GILGFVFTL SEQ ID NO. 8 - reactive with influenze-specific CTLs (Gammon et al., 1992 J Immunol. 148, 7-12) were 5'-labelled with ^{32}P using polynucleotide kinase and ^{32}P ATP and annealed together, self-ligated at 37°C for 4 hours using T4 DNA ligase (Life Technologies, Paisley UK) and analysed on a preparative polyacrylamide sequencing gel. The bands at 180 base pairs representing 5 self-ligated copies of P53-U/L or FLU-U/L were purified, ligated to phosphorylated NotI linkers (#1127), New England Biolabs, Hitchin, UK) and digested with NotI (Pharmacia).

Please replace the paragraph on the bottom of page 11 and the top of page 12 with the following paragraph:

For preparaton of cytotoxic T lymphocytes (CTLs) specific for the p53-derived peptide as above, the in vivo mouse peptide immunization and sensitization procedure of Noguchi et al. (loc. cit.) was followed to produce long-term CTL lines. For testing of antibodies for ability to induce CTL activity, target mouse Sp2/0 cells (ATCC CRL-1581) were used and maintained in DMEM and

10% foetal bovine serum. For CTL assays, cells at 5 x 10^5 cells/ml were labeled overnight with 20µCi (7.4MBq) ^{51}Cr chromate. Cells were then pelleted, washed in medium and resuspended at 5 x 10^5 cells/ml in medium plus dilutions of the antibody fragments or 10µg/ml peptide KYICNSSCM SEQ ID NO. 7 ("p53 peptide only") for 4 hours at 37°C. Cells were then repelleted, washed twice in PBS (phosphate-buffered saline) and plated at 5 x 10^5 cells in 100µl in RPMI1640 medium plus 10% foetal bovine serum in 24-well plates. 100µl of CTLs were then added to give effector:target ratios of 20:1, 10:1 and 5:1 and incubated for 4 hours at 37°C. After incubation, 100µl of cluture supernatant was carefully removed from each well into an eppendorf tube, centrifuged and triplicate 20µl aliquots of supernatant were counted in a scintillation counter. Percent specific release was calculated as [(release by effector cells-spontaneous release)/(maximum release-spontaneous release)]x100. Results were as follows:...

On page 13, please replace the second paragraph with the following paragraph:

Human cytotoxic T lymphocyte (CTLs) specific for the flu peptide GILGFVFTL SEQ ID NO. 8 were obtained from a normal HLA-A2 donor and were maintained as described by Bednarea et al., (1991 J. Immunological Methods 139, 41-47). Testing of antibodies for ability to induce CTL activity against target MCF7 cells was as

for example 1 with effector:target ratios of 40:1, 20:1 and 10:1.

Results were as follows:...

Marked-up Version of Claims Being Amended

1(Amended). A chimaeric polypeptide comprising:

(a) [a binding portion comprising at least a portion of an immunoglobulin molecule] a scFv having specific binding affinity for a eucaryotic target cell surface component;

(b) an effector portion [consisting of] comprising at least one copy of an immunogenic peptide having the sequence KYICNSSCM or GILGFVFTL; and optionally

(c) a signal [from another source] derived from the translocation domain of HIV tat protein directing the immunogenic peptide to a particular cellular component, whereby binding of the chimaeric polypeptide to the cell surface component induces internalisation of at least the effector portion to allow the at least one copy of the immunogenic peptide to be presented by MHC molecules on the target cell surface.

2. A chimaeric polypeptide comprising: a [binding portion] scFv, from a first source, having specific binding affinity for a eukaryotic target cell surface component; an effector portion, from a second source, comprising [a peptide which exerts an immunomodulatory effect]; at least one copy of an immunogenic peptide having the sequence KYICNSSCM or GILGFVFTL, and a translocation portion [from a third source] derived from the

translocation domain of HIV tat protein, the translocation portion being adjacent to the effector portion; whereby binding of the polypeptide to the cell surface component induces internalization of at least the effector and translocation portions so as to allow the effector portion to enter the cytosol of the target cell and hence all the peptide [exert its immunomodulatory effect] to induce cell lysis.

Rewrite claim 9 as follows:

9(Amended). A polypeptide according to claim 1 or 2 wherein the effector portion comprises a number of repeats of the same peptide [which exerts an immunomodulatory effect].

Rewrite claims 21 and 23 as follows:

21(Amended). A method of [modulating the immune response] stimulating cell lysis of a human or animal subject, comprising administering to the subject an effective amount of a polypeptide in accordance with claim 1 or 2.

23(Amended). A method according to claim 22, wherein administering the polypeptide causes the target cell to present a CTL epitope which is foreign to the [subject] target cell.